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CCR4 mutations associated with superior outcome of adult T-cell leukemia/lymphoma under mogamulizumab treatment

ABSTRACT

Adult T-cell leukemia/lymphoma (ATL) has a dismal prognosis. CCR4 is expressed by tumor cells from most ATL patients, so therapeutic antibodies such as mogamulizumab, may be effective treatments. Here, we investigate whether gain-of-function mutations in the carboxyl terminus of CCR4, which were observed in 38 (33%) of 116 ATL patients, influence overall survival (OS) and response to treatment. We found no significant differences in OS when the whole patient cohort was stratified according to *CCR4* mutations. However, in those receiving mogamulizumab, 5-year survival from initiation of treatment in patients with (n = 11) or without (n = 31) *CCR4* mutations was 72.7% and 26.2%, respectively ($P = 0.027$). In contrast, *CCR4* mutations did not influence the outcome of allogeneic hematopoietic stem cell transplantation. Finally, in patients with aggressive-variant ATL, 5-year survival on mogamulizumab for patients with (n = 10) or without (n = 28) *CCR4* mutations was 80.0% and 24.7%, respectively ($P = 0.006$). These findings suggest that ATL patients with gain-of-function *CCR4* mutations are especially good responders to mogamulizumab-containing treatments. Thus, we conclude that *CCR4* gain-of-function mutations determine sensitivity to mogamulizumab therapy in ATL.